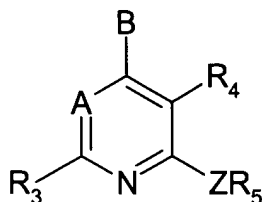


1. (previously presented) A compound of the formula



1

**A is N:**

Z is NH, O, S, -N(C<sub>1</sub>-C<sub>2</sub> alkyl), -NC(O)CF<sub>3</sub>, or -C(R<sub>13</sub>R<sub>14</sub>), wherein R<sub>13</sub> and R<sub>14</sub> are each, independently, hydrogen, trifluoromethyl or methyl, or one of R<sub>13</sub> and R<sub>14</sub> is cyano and the other is hydrogen or methyl, or -C(R<sub>13</sub>R<sub>14</sub>) is a cyclopropyl group, or Z is nitrogen or CH and forms a five or six membered heterocyclic ring fused with R<sub>5</sub>, which ring optionally comprises two or three further members selected independently from oxygen, nitrogen, NR<sub>12</sub>, and S(O)<sub>m</sub>, and optionally comprises from one to three double bonds, and is optionally substituted with halo, C<sub>1</sub>-C<sub>4</sub> alkyl, -C<sub>4</sub> alkyl), NH<sub>2</sub>, NHCH<sub>3</sub>, N(CH<sub>3</sub>)<sub>2</sub>, CF<sub>3</sub>, or OCF<sub>3</sub>, with the proviso that said ring does not contain -S-, -S-O-, -N-S-, or -O-O- bonds, and does not comprise more than two oxygen or S(O)<sub>m</sub> homologous members;

R<sub>1</sub> is C(O)H, C(O)(C<sub>1</sub>-C<sub>6</sub> hydrocarbyl), C(O)(C<sub>1</sub>-C<sub>6</sub> hydrocarbylene)(C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbyl), C(O)(C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbylene)(C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbyl), C(O)(C<sub>1</sub>-C<sub>6</sub> hydrocarbylene)(C<sub>4</sub>-C<sub>8</sub> heterocyclohydrocarbyl), -C(O)(C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbylene)(C<sub>4</sub>-C<sub>8</sub> heterocyclohydrocarbyl), C<sub>1</sub>-C<sub>6</sub> hydrocarbyl, C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbyl, C<sub>4</sub>-C<sub>8</sub> heterocyclohydrocarbyl, -(C<sub>1</sub>-C<sub>6</sub> hydrocarbylene)(C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbyl), -(C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbylene)(C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbyl), -(C<sub>1</sub>-C<sub>6</sub> hydrocarbylene)(C<sub>4</sub>-C<sub>8</sub> heterocyclohydrocarbyl), -(C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbylene)(C<sub>4</sub>-C<sub>8</sub> heterocyclohydrocarbyl), or -O-aryl, or -O-(C<sub>1</sub>-C<sub>6</sub> hydrocarbylene)-aryl; wherein said aryl, C<sub>4</sub>-C<sub>8</sub> heterocyclohydrocarbyl, C<sub>1</sub>-C<sub>6</sub> hydrocarbyl, C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbyl, C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbylene, and C<sub>1</sub>-C<sub>6</sub> hydrocarbylene groups may each independently be optionally substituted with from one to six fluoro and may each independently be optionally substituted with one or two substituents R<sub>8</sub> independently selected from the group consisting of C<sub>1</sub>-C<sub>4</sub> hydrocarbyl, -C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbyl, hydroxy, chloro, bromo, iodo, CF<sub>3</sub>, -O-(C<sub>1</sub>-C<sub>6</sub> hydrocarbyl), -O-(C<sub>3</sub>-C<sub>5</sub> cyclohydrocarbyl), -O-CO-(C<sub>1</sub>-

C<sub>4</sub> hydrocarbyl), -O-CO-NH(C<sub>1</sub>-C<sub>4</sub> hydrocarbyl), -O-CO-N(R<sub>24</sub>)(R<sub>25</sub>), -N(R<sub>24</sub>)(R<sub>25</sub>), -S(C<sub>1</sub>-C<sub>4</sub> hydrocarbyl), -S(C<sub>3</sub>-C<sub>5</sub> cyclohydrocarbyl), -N(C<sub>1</sub>-C<sub>4</sub> hydrocarbyl)CO(C<sub>1</sub>-C<sub>4</sub> hydrocarbyl), -NHCO(C<sub>1</sub>-C<sub>4</sub> hydrocarbyl), -COO(C<sub>1</sub>-C<sub>4</sub> hydrocarbyl), -CONH(C<sub>1</sub>-C<sub>4</sub> hydrocarbyl), -CON(C<sub>1</sub>-C<sub>4</sub> hydrocarbyl)(C<sub>1</sub>-C<sub>2</sub> hydrocarbyl), CN, NO<sub>2</sub>, -OSO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> hydrocarbyl), S<sup>+</sup>(C<sub>1</sub>-C<sub>6</sub> hydrocarbyl)(C<sub>1</sub>-C<sub>2</sub> hydrocarbyl)I<sup>-</sup>, -SO(C<sub>1</sub>-C<sub>4</sub> hydrocarbyl) and -SO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> hydrocarbyl); and wherein the C<sub>1</sub>-C<sub>6</sub> hydrocarbyl, C<sub>1</sub>-C<sub>6</sub> hydrocarbylene, C<sub>5</sub>-C<sub>8</sub> cyclohydrocarbyl, C<sub>5</sub>-C<sub>8</sub> cyclohydrocarbylene, and C<sub>5</sub>-C<sub>8</sub> heterocyclohydrocarbyl moieties of R<sub>1</sub> may optionally independently contain from one to three double or triple bonds; and wherein the C<sub>1</sub>-C<sub>4</sub> hydrocarbyl moieties and C<sub>1</sub>-C<sub>6</sub> hydrocarbyl moieties of R<sub>8</sub> can optionally independently be substituted with hydroxy, amino, C<sub>1</sub>-C<sub>4</sub> hydrocarbyl, aryl, -CH<sub>2</sub>-aryl, C<sub>3</sub>-C<sub>5</sub> cyclohydrocarbyl, or -O-(C<sub>1</sub>-C<sub>4</sub> hydrocarbyl), and can optionally independently be substituted with from one to six fluoro, and can optionally contain one or two double or triple bonds; and wherein each heterocyclohydrocarbyl group of R<sub>1</sub> contains from one to three heteromoiety selected from oxygen, S(O)<sub>m</sub>, nitrogen, and NR<sub>12</sub>;

R<sub>2</sub> is hydrogen, C<sub>1</sub>-C<sub>12</sub> hydrocarbyl, C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbyl, C<sub>4</sub>-C<sub>8</sub> heterocyclohydrocarbyl, -(C<sub>1</sub>-C<sub>6</sub> hydrocarbylene)(C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbyl), -(C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbylene)(C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbyl), -(C<sub>1</sub>-C<sub>6</sub> hydrocarbylene)(C<sub>4</sub>-C<sub>8</sub> heterocyclohydrocarbyl), -(C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbylene)(C<sub>4</sub>-C<sub>8</sub> heterocyclohydrocarbyl), aryl, -(C<sub>1</sub>-C<sub>6</sub> hydrocarbylene)aryl, or -(C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbylene)(aryl); wherein each of the foregoing R<sub>2</sub> groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, and C<sub>1</sub>-C<sub>6</sub> hydrocarbyl, wherein one of said one to three substituents can further be selected from bromo, iodo, C<sub>1</sub>-C<sub>6</sub> alkoxy, -OH, -O-CO-(C<sub>1</sub>-C<sub>6</sub> hydrocarbyl), -O-CO-N(C<sub>1</sub>-C<sub>4</sub> hydrocarbyl)(C<sub>1</sub>-C<sub>2</sub> hydrocarbyl), -S(C<sub>1</sub>-C<sub>6</sub> hydrocarbyl), -S(O)(C<sub>1</sub>-C<sub>6</sub> hydrocarbyl), -S(O)<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> hydrocarbyl), S<sup>+</sup>(C<sub>1</sub>-C<sub>6</sub> hydrocarbyl)(C<sub>1</sub>-C<sub>2</sub> hydrocarbyl)I<sup>-</sup>, CN, and NO<sub>2</sub>; and wherein the C<sub>1</sub>-C<sub>12</sub> hydrocarbyl, -(C<sub>1</sub>-C<sub>6</sub> hydrocarbylene), and cyclohydrocarbyl groups of 5 - 8 carbon atoms, cyclohydrocarbylene groups of 5 to 8 carbon atoms and heterocyclohydrocarbyl groups of 5 to 8 atoms of R<sub>2</sub> may optionally independently contain from one to three double or triple bonds; and wherein each heterocyclohydrocarbyl group of R<sub>2</sub> contains from one to three heteromoiety selected from oxygen, S(O)<sub>m</sub>, nitrogen, and NR<sub>12</sub>;

or when R<sub>1</sub> and R<sub>2</sub> are as in -NHCHR<sub>1</sub>R<sub>2</sub>, -OCHR<sub>1</sub>R<sub>2</sub>, -SCHR<sub>1</sub>R<sub>2</sub>, -CHR<sub>1</sub>R<sub>2</sub> or -NR<sub>1</sub>R<sub>2</sub>, R<sub>1</sub> and R<sub>2</sub> of B may form a saturated 5- to 8-membered ring which may optionally contain one or two double bonds and in which one or two of the ring carbons may optionally be replaced by an oxygen, S(O)<sub>m</sub>, nitrogen or NR<sub>12</sub>; and which carbocyclic ring can optionally be substituted with from 1 to 3 substituents selected from the group consisting of hydroxy, C<sub>1</sub>-C<sub>4</sub> alkyl, fluoro, chloro, bromo, iodo, CF<sub>3</sub>, -O-(C<sub>1</sub>-C<sub>4</sub> alkyl), -O-CO-(C<sub>1</sub>-C<sub>4</sub> alkyl), -O-CO-NH(C<sub>1</sub>-C<sub>4</sub> alkyl), -O-CO-N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), -NH(C<sub>1</sub>-C<sub>4</sub> alkyl), -N(C<sub>1</sub>-C<sub>2</sub> alkyl)(C<sub>1</sub>-C<sub>4</sub> alkyl), -S(C<sub>1</sub>-C<sub>4</sub> alkyl), -N(C<sub>1</sub>-C<sub>4</sub> alkyl)CO(C<sub>1</sub>-C<sub>4</sub> alkyl), -NHCO(C<sub>1</sub>-C<sub>4</sub> alkyl), -COO(C<sub>1</sub>-C<sub>4</sub> alkyl), -CONH(C<sub>1</sub>-C<sub>4</sub> alkyl), -CON(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), CN,

NO<sub>2</sub>, -OSO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), -SO(C<sub>1</sub>-C<sub>4</sub> alkyl), and -SO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), wherein one of said one to three substituents can further be selected from phenyl;

R<sub>3</sub> is methyl, ethyl, fluoro, chloro, bromo, iodo, cyano, methoxy, OCF<sub>3</sub>, NH<sub>2</sub>, NH(C<sub>1</sub>-C<sub>2</sub> alkyl), N(CH<sub>3</sub>)<sub>2</sub>, -NHCOCF<sub>3</sub>, -NHCH<sub>2</sub>CF<sub>3</sub>, S(O)<sub>m</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), CONH<sub>2</sub>, -CONHCH<sub>3</sub>, CON(CH<sub>3</sub>)<sub>2</sub>, -CF<sub>3</sub>, or CH<sub>2</sub>OCH<sub>3</sub>;

R<sub>4</sub> is hydrogen, C<sub>1</sub>-C<sub>4</sub> hydrocarbyl, C<sub>3</sub>-C<sub>5</sub> cycloalkyl, -(C<sub>1</sub>-C<sub>4</sub> hydrocarbylene)(C<sub>3</sub>-C<sub>5</sub> cycloalkyl), -(C<sub>3</sub>-C<sub>5</sub> cycloalkylene)(C<sub>3</sub>-C<sub>5</sub> cycloalkyl), cyano, fluoro, chloro, bromo, iodo, -OR<sub>24</sub>, C<sub>1</sub>-C<sub>6</sub> alkoxy, -O-(C<sub>3</sub>-C<sub>5</sub> cycloalkyl), -O-(C<sub>1</sub>-C<sub>4</sub> hydrocarbylene)(C<sub>3</sub>-C<sub>5</sub> cycloalkyl), -O-(C<sub>3</sub>-C<sub>5</sub> cycloalkylene)(C<sub>3</sub>-C<sub>5</sub> cycloalkyl), -CH<sub>2</sub>SC(S)O(C<sub>1</sub>-C<sub>4</sub> hydrocarbyl), -CH<sub>2</sub>OF<sub>3</sub>, CF<sub>3</sub>, amino, nitro, -NR<sub>24</sub>R<sub>25</sub>, -(C<sub>1</sub>-C<sub>4</sub> hydrocarbylene)-OR<sub>24</sub>, -(C<sub>1</sub>-C<sub>4</sub> hydrocarbylene)Cl, -(C<sub>1</sub>-C<sub>4</sub> hydrocarbylene)NR<sub>24</sub>R<sub>25</sub>, -NHCOR<sub>24</sub>, -NHCONR<sub>24</sub>R<sub>25</sub>, -C=NOR<sub>24</sub>, -NHNOR<sub>24</sub>R<sub>25</sub>, -S(O)<sub>m</sub>R<sub>24</sub>, -C(O)R<sub>24</sub>, -OC(O)R<sub>24</sub>, -C(O)CN, -C(O)NR<sub>24</sub>R<sub>25</sub>, -C(O)NHNOR<sub>24</sub>R<sub>25</sub>, and -COOR<sub>24</sub>, wherein the hydrocarbyl and hydrocarbylene groups of R<sub>4</sub> may optionally independently contain one or two double or triple bonds and may optionally independently be substituted with one or two substituents R<sub>10</sub> independently selected from hydroxy, amino, -NHCOCH<sub>3</sub>, -NHCOCH<sub>2</sub>Cl, -NH(C<sub>1</sub>-C<sub>2</sub> alkyl), -N(C<sub>1</sub>-C<sub>2</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), -COO(C<sub>1</sub>-C<sub>4</sub> alkyl), -COOH, -CO(C<sub>1</sub>-C<sub>4</sub> alkyl), C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>3</sub> thioalkyl, cyano and nitro, and with one to four substituents independently selected from fluoro and chloro;

R<sub>5</sub> is aryl or heteroaryl and is substituted with from one to four substituents R<sub>27</sub> independently selected from halo, C<sub>1</sub>-C<sub>10</sub> alkyl, -(C<sub>1</sub>-C<sub>4</sub> alkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), -(C<sub>1</sub>-C<sub>4</sub> alkylene)(C<sub>4</sub>-C<sub>8</sub> heterocycloalkyl), -(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), -(C<sub>4</sub>-C<sub>8</sub> heterocycloalkyl), -(C<sub>3</sub>-C<sub>8</sub> cycloalkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), -(C<sub>3</sub>-C<sub>8</sub> cycloalkylene)(C<sub>4</sub>-C<sub>8</sub> heterocycloalkyl), C<sub>1</sub>-C<sub>4</sub> haloalkyl, C<sub>1</sub>-C<sub>4</sub> haloalkoxy, nitro, cyano, -NR<sub>24</sub>R<sub>25</sub>, -NR<sub>24</sub>COR<sub>25</sub>, -NR<sub>24</sub>CO<sub>2</sub>R<sub>26</sub>, -COR<sub>24</sub>, -OR<sub>25</sub>, -CONR<sub>24</sub>R<sub>25</sub>, -CO(NOR<sub>22</sub>)R<sub>23</sub>, -CO<sub>2</sub>R<sub>26</sub>, -C=N(OR<sub>22</sub>)R<sub>23</sub>, and -S(O)<sub>m</sub>R<sub>23</sub>; wherein said C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, (C<sub>1</sub>-C<sub>4</sub> alkylene), (C<sub>3</sub>-C<sub>8</sub> cycloalkyl), (C<sub>3</sub>-C<sub>8</sub> cycloalkylene), and (C<sub>4</sub>-C<sub>8</sub> heterocycloalkyl) groups can be optionally substituted with from one to three substituents independently selected from C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, (C<sub>1</sub>-C<sub>4</sub> alkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), -(C<sub>3</sub>-C<sub>8</sub> cycloalkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), C<sub>1</sub>-C<sub>4</sub> haloalkyl, hydroxy, C<sub>1</sub>-C<sub>6</sub> alkoxy, nitro halo, cyano, -NR<sub>24</sub>R<sub>25</sub>, -NR<sub>24</sub>COR<sub>25</sub>, -NR<sub>24</sub>CO<sub>2</sub>R<sub>26</sub>, -COR<sub>24</sub>, -OR<sub>25</sub>, -CONR<sub>24</sub>R<sub>25</sub>, CO<sub>2</sub>R<sub>26</sub>, -CO(NOR<sub>22</sub>)R<sub>25</sub>, and -S(O)<sub>m</sub>R<sub>23</sub>; and wherein two adjacent substituents of the R<sub>5</sub> group can optionally form a 5-7 membered ring, saturated or unsaturated, fused to R<sup>5</sup>, which ring optionally can contain one, two, or three heterologous members independently selected from O, S(O)<sub>m</sub>, and N, but not any -S-S-, -O-O-, -S-O-, or -N-S- bonds, and which ring is optionally substituted with C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, -(C<sub>1</sub>-C<sub>4</sub> alkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), -(C<sub>3</sub>-C<sub>8</sub> cycloalkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), C<sub>1</sub>-C<sub>4</sub> haloalkyl, nitro, halo, cyano -NR<sub>24</sub>R<sub>25</sub>, -NR<sub>24</sub>COR<sub>25</sub>, -NR<sub>24</sub>CO<sub>2</sub>R<sub>26</sub>, -COR<sub>24</sub>, -OR<sub>25</sub>, -CONR<sub>24</sub>R<sub>25</sub>, CO<sub>2</sub>R<sub>26</sub>, -CO(NOR<sub>26</sub>)R<sub>25</sub>, or -S(O)<sub>m</sub>R<sub>23</sub>; wherein one of said one to four optional substituents R<sub>27</sub> can further be selected from -SO<sub>2</sub>NH(C<sub>1</sub>-C<sub>4</sub> alkyl), -SO<sub>2</sub>NH(C<sub>1</sub>-C<sub>4</sub> alkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), -SO<sub>2</sub>NH(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), -SO<sub>2</sub>NH(C<sub>3</sub>-C<sub>8</sub> cycloalkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), -SO<sub>2</sub>N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub>

alkyl), -SO<sub>2</sub>NH<sub>2</sub>, -NHSO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), -NHSO<sub>2</sub>(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), -NHSO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), and -NHSO<sub>2</sub>(C<sub>3</sub>-C<sub>8</sub> cycloalkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl); and wherein the alkyl, and alkylene groups of R<sub>5</sub> may independently optionally contain one double or triple bond;

R<sub>11</sub> is hydrogen, hydroxy, fluoro, ethoxy, or methoxy;

R<sub>12</sub> is hydrogen or C<sub>1</sub>-C<sub>4</sub> alkyl;

R<sub>22</sub> is independently at each occurrence selected from hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> haloalkyl, C<sub>3</sub>-C<sub>8</sub> alkenyl, C<sub>3</sub>-C<sub>8</sub> alkynyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, (C<sub>3</sub>-C<sub>8</sub> cycloalkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), and (C<sub>1</sub>-C<sub>4</sub> alkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl);

R<sub>23</sub> is independently at each occurrence selected from C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> haloalkyl, C<sub>2</sub>-C<sub>8</sub> alkoxyalkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, -(C<sub>1</sub>-C<sub>4</sub> alkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), -(C<sub>3</sub>-C<sub>8</sub> cycloalkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), aryl, -(C<sub>1</sub>-C<sub>4</sub> alkylene)aryl, piperidine, pyrrolidine, piperazine, N-methylpiperazine, morpholine, and thiomorpholine;

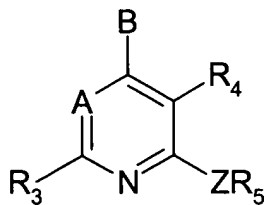
R<sub>24</sub> and R<sub>25</sub> are independently at each occurrence selected from hydrogen, -C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> haloalkyl, especially CF<sub>3</sub>, -CHF<sub>2</sub>, CF<sub>2</sub>CF<sub>3</sub>, or CH<sub>2</sub>CF<sub>3</sub>, -(C<sub>1</sub>-C<sub>4</sub> alkylene)OH, -(C<sub>1</sub>-C<sub>4</sub> alkylene)-O-(C<sub>1</sub>-C<sub>4</sub> alkyl), -(C<sub>1</sub>-C<sub>4</sub> alkylene)-O-(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), C<sub>3</sub>-C<sub>8</sub> cycloalkyl, -(C<sub>1</sub>-C<sub>4</sub> alkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), -(C<sub>3</sub>-C<sub>8</sub> cycloalkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), -C<sub>4</sub>-C<sub>8</sub> heterocyclohydrocarbyl, -(C<sub>1</sub>-C<sub>4</sub> alkylene)(C<sub>4</sub>-C<sub>8</sub> heterocyclohydrocarbyl), -(C<sub>3</sub>-C<sub>8</sub> cycloalkylene)(C<sub>4</sub>-C<sub>8</sub> heterocyclohydrocarbyl), aryl, and -(C<sub>1</sub>-C<sub>4</sub> alkylene)(aryl), wherein the -C<sub>4</sub>-C<sub>8</sub> heterocyclohydrocarbyl groups can each independently optionally be substituted with aryl, CH<sub>2</sub>-aryl, or C<sub>1</sub>-C<sub>4</sub> alkyl, and can optionally contain one or two double or triple bonds; or, when R<sub>24</sub> and R<sub>25</sub> are as NR<sub>24</sub>R<sub>25</sub>, -C(O)NR<sub>24</sub>R<sub>25</sub>, -(C<sub>1</sub>-C<sub>4</sub> alkylene)NR<sub>24</sub>R<sub>25</sub>, or -NHCONR<sub>24</sub>R<sub>25</sub>, then NR<sub>24</sub>R<sub>25</sub> may further optionally form a 4 to 8 membered heterocyclic ring optionally containing one or two further hetero members independently selected from S(O)<sub>m</sub>, oxygen, nitrogen, and NR<sub>12</sub>, and optionally containing from one to three double bonds;

R<sub>26</sub> is independently at each occurrence selected from C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> haloalkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, -(C<sub>1</sub>-C<sub>4</sub> alkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), -(C<sub>3</sub>-C<sub>8</sub> cycloalkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), aryl, and -(C<sub>1</sub>-C<sub>4</sub> alkylene)(aryl); and

wherein each m is independently zero, one, or two,

with the proviso that heterocycloalkyl groups of the compound of formula I, II, or III do not comprise any -S-S-, -S-O-, -N-S-, or -O-O- bonds, and do not comprise more than two oxygen or S(O)<sub>m</sub> heterologous members.

2. (previously presented) A compound according to claim 1 of the formula



I

, wherein

A is N;

B

is  $-NR_1R_2$ ,  $-CR_1R_2R_{11}$ ,  $-C(=CR_2R_{12})R_1$ ,  $-NHCHR_1R_2$ ,  $-OCHR_1R_2$ ,  $-SCHR_1R_2$ ,  $-CHR_2OR_{12}$ ,  $-CHR_2SR_1$ ,  $-C(S)R_2$  or  $-C(O)R_2$ ;

Z is NH, O, S,  $-N(C_1-C_2 \text{ alkyl})$  or  $-C(R_{13}R_{14})$ , wherein  $R_{13}$  and  $R_{14}$  are each, independently, hydrogen, trifluoromethyl or methyl, or one of  $R_{13}$  and  $R_{14}$  is cyano and the other is hydrogen or methyl;

$R_1$  is  $C_1-C_6$  hydrocarbyl which may optionally be substituted with one or two substituents  $R_8$  independently selected from the group consisting of hydroxy, fluoro, chloro, bromo, iodo,  $CF_3$ ,  $C_1-C_4$  alkoxy,  $-O-CO-(C_1-C_4 \text{ hydrocarbyl})$ ,  $-O-CO-NH(C_1-C_4 \text{ hydrocarbyl})$ ,  $-O-CO-N(C_1-C_4 \text{ hydrocarbyl})(C_1-C_2 \text{ hydrocarbyl})$ ,  $-NH(C_1-C_4 \text{ hydrocarbyl})$ ,  $-N(C_1-C_2 \text{ hydrocarbyl})(C_1-C_4 \text{ hydrocarbyl})$ ,  $-S(C_1-C_4 \text{ hydrocarbyl})$ ,  $-N(C_1-C_4 \text{ hydrocarbyl})CO(C_1-C_4 \text{ hydrocarbyl})$ ,  $-NHCO(C_1-C_4 \text{ hydrocarbyl})$ ,  $-COO(C_1-C_4 \text{ hydrocarbyl})$ ,  $-CONH(C_1-C_4 \text{ hydrocarbyl})$ ,  $-CON(C_1-C_4 \text{ hydrocarbyl})(C_1-C_2 \text{ alkyl})$ , CN,  $NO_2$ ,  $-SO(C_1-C_4 \text{ hydrocarbyl})$  and  $-SO_2(C_1-C_4 \text{ hydrocarbyl})$ , and wherein said  $C_1-C_6$  hydrocarbyl and the  $(C_1-C_4)$ hydrocarbyl moieties in the foregoing  $R_1$  groups may optionally contain one carbon-carbon double or triple bond;

$R_2$  is  $C_1-C_{12}$  hydrocarbyl, aryl or  $-(C_1-C_4 \text{ hydrocarbylene})\text{aryl}$  wherein said aryl is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, benzisothiazolyl, benzisoxazolyl, benzimidazolyl, indolyl, or benzoxazolyl; 3- to 8-membered cycloalkyl or  $-(C_1-C_6 \text{ alkylene})\text{cycloalkyl}$ , wherein one or two of the ring carbons of said cycloalkyl having at least 4 ring members and the cycloalkyl moiety of said  $-(C_1-C_6 \text{ alkylene})\text{cycloalkyl}$  having at least 4 ring members may optionally be replaced by an oxygen or sulfur atom or by  $N-R_9$  wherein  $R_9$  is hydrogen or  $C_1-C_4$  alkyl; and wherein each of the foregoing  $R_2$  groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro and  $C_1-C_4$  alkyl, or with one substituent selected from bromo, iodo,  $C_1-C_6$  alkoxy,  $-O-CO-(C_1-C_6 \text{ alkyl})$ ,  $-O-CO-N(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl})$ ,  $-S(C_1-C_6 \text{ alkyl})$ , CN,  $NO_2$ ,  $-SO(C_1-C_4 \text{ alkyl})$ , and  $-SO_2(C_1-C_4 \text{ alkyl})$ , and wherein said  $C_1-C_{12}$  hydrocarbyl and the  $C_1-C_4$  hydrocarbylene moiety of said  $-(C_1-C_4 \text{ hydrocarbylene})\text{aryl}$  may optionally contain one carbon-carbon double or triple bond;

or  $-NR_1R_2$  or  $-CR_1R_2R_{11}$  may form a saturated 5- to 8-membered carbocyclic ring which may optionally contain one or two carbon-carbon double bonds and in which one or two of the ring carbons may optionally be replaced by an oxygen or sulfur atom;

R<sub>3</sub> is methyl, ethyl, fluoro, chloro, bromo, iodo, cyano, methoxy, OCF<sub>3</sub>, methylthio, methylsulfonyl, CH<sub>2</sub>OH, or CH<sub>2</sub>OCH<sub>3</sub>;

R<sub>4</sub> is hydrogen, C<sub>1</sub>-C<sub>4</sub> hydrocarbyl, fluoro, chloro, bromo, iodo, C<sub>1</sub>-C<sub>4</sub> alkoxy, trifluoromethoxy, -CH<sub>2</sub>OCH<sub>3</sub>, -CH<sub>2</sub>OCH<sub>2</sub>CH<sub>3</sub>, -CH<sub>2</sub>CH<sub>2</sub>OCH<sub>3</sub>, -CH<sub>2</sub>OF<sub>3</sub>, CF<sub>3</sub>, amino, nitro, -NH(C<sub>1</sub>-C<sub>4</sub> alkyl), -N(CH<sub>3</sub>)<sub>2</sub>, -NHCOCH<sub>3</sub>, -NHCONHCH<sub>3</sub>, -SO<sub>n</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl) wherein n is 0, 1 or 2, cyano, hydroxy, -CO(C<sub>1</sub>-C<sub>4</sub> alkyl), -CHO, cyano or -COO(C<sub>1</sub>-C<sub>4</sub> alkyl) wherein said C<sub>1</sub>-C<sub>4</sub> hydrocarbyl may optionally contain one double or triple bond and may optionally be substituted with one substituent selected from hydroxy, amino, -NHCOCH<sub>3</sub>, -NH(C<sub>1</sub>-C<sub>2</sub> alkyl), -N(C<sub>1</sub>-C<sub>2</sub> alkyl)<sub>2</sub>, -COO(C<sub>1</sub>-C<sub>4</sub> alkyl), -CO(C<sub>1</sub>-C<sub>4</sub> alkyl), C<sub>1</sub>-C<sub>3</sub> alkoxy, C<sub>1</sub>-C<sub>3</sub> thioalkyl, fluoro, chloro, cyano and nitro;

R<sub>5</sub> is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, furanyl, benzofuranyl, benzothiazolyl, or indolyl, wherein each of the above groups R<sub>5</sub> is substituted with from one to three substituents independently selected from fluoro, chloro, C<sub>1</sub>-C<sub>6</sub> alkyl, and C<sub>1</sub>-C<sub>6</sub> alkoxy, or with one substituent selected from hydroxy, iodo, bromo, formyl, cyano, nitro, trifluoromethyl, amino, -(C<sub>1</sub>-C<sub>6</sub> alkyl)O(C<sub>1</sub>-C<sub>6</sub>)alkyl, -NHCH<sub>3</sub>, -N(CH<sub>3</sub>)<sub>2</sub>, -COOH, -COO(C<sub>1</sub>-C<sub>4</sub> alkyl), -CO(C<sub>1</sub>-C<sub>4</sub> alkyl), -SO<sub>2</sub>NH(C<sub>1</sub>-C<sub>4</sub> alkyl), -SO<sub>2</sub>N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), -SO<sub>2</sub>NH<sub>2</sub>, -NHSO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), -S(C<sub>1</sub>-C<sub>6</sub> alkyl) and -SO<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), and wherein the C<sub>1</sub>-C<sub>4</sub> alkyl and C<sub>1</sub>-C<sub>6</sub> alkyl moieties of the foregoing R<sub>5</sub> groups may optionally be substituted with one or two fluoro groups or with one substituent selected from hydroxy, amino, methylamino, dimethylamino and acetyl;

R<sub>11</sub> is hydrogen, hydroxy, fluoro, or methoxy;

R<sub>12</sub> is hydrogen or C<sub>1</sub>-C<sub>4</sub> alkyl; and

or a pharmaceutically acceptable salt of such compound.

3. (previously presented) A compound according to claim 2 wherein B is -NR<sub>1</sub>R<sub>2</sub>, -NHCHR<sub>1</sub>R<sub>2</sub>, -SCHR<sub>1</sub>R<sub>2</sub> or -OCHR<sub>1</sub>R<sub>2</sub>; R<sub>1</sub> is C<sub>1</sub>-C<sub>6</sub> hydrocarbyl, which may optionally be substituted with one hydroxy, fluoro, CF<sub>3</sub>, or C<sub>1</sub>-C<sub>2</sub> alkoxy group and may optionally contain one double or triple bond; and R<sub>2</sub> is benzyl or C<sub>1</sub>-C<sub>6</sub> alkyl which may optionally contain one carbon-carbon double or triple bond, wherein said C<sub>1</sub>-C<sub>6</sub> alkyl or the phenyl moiety of said benzyl may optionally be substituted with fluoro, CF<sub>3</sub>, C<sub>1</sub>-C<sub>2</sub> alkyl, or C<sub>1</sub>-C<sub>2</sub> alkoxy.

4. (previously presented) A compound according to claim 2 wherein R<sub>1</sub> is C<sub>1</sub>-C<sub>6</sub> hydrocarbyl which may be substituted by fluoro, CF<sub>3</sub>, hydroxy, C<sub>1</sub>-C<sub>2</sub> alkyl or C<sub>1</sub>-C<sub>2</sub> alkoxy and which may optionally contain one carbon-carbon double or triple bond.

5. (previously presented) A compound according to claim 2 wherein R<sub>2</sub> is C<sub>1</sub>-C<sub>4</sub> alkyl which may optionally be substituted by fluoro, chloro, CF<sub>3</sub>, C<sub>1</sub>-C<sub>4</sub> alkyl or C<sub>1</sub>-C<sub>4</sub> alkoxy.

6. (previously presented) A compound according to claim 2 wherein R<sub>3</sub> is methyl, chloro, or methoxy.

7. (previously presented) A compound according to claim 2 wherein R<sub>4</sub> is methyl, -CH<sub>2</sub>OH, cyano, trifluoromethoxy, methoxy, chloro, trifluoromethyl, -COOCH<sub>3</sub>, -CH<sub>2</sub>OCH<sub>3</sub>, -CH<sub>2</sub>Cl, -CH<sub>2</sub>F, ethyl, amino or nitro.

8. (previously presented) A compound according to claim 2 wherein R<sub>5</sub> is phenyl substituted with two or three substituents.

9. (previously presented) A compound according to claim 2 wherein R<sub>5</sub> is pyridyl substituted with two or three substituents.

10. (previously presented) A compound according to claim 8 wherein said substituents are selected, independently, from fluoro, chloro, bromo, iodo, C<sub>1</sub>-C<sub>4</sub> alkoxy, trifluoromethyl, C<sub>1</sub>-C<sub>6</sub> alkyl which may optionally be substituted with one hydroxy, C<sub>1</sub>-C<sub>4</sub> alkoxy or fluoro group and which may optionally contain one carbon-carbon double or triple bond, -(C<sub>1</sub>-C<sub>4</sub> alkylene)O(C<sub>1</sub>-C<sub>2</sub> alkyl), C<sub>1</sub>-C<sub>3</sub> hydroxyalkyl, hydroxy, formyl, COO(C<sub>1</sub>-C<sub>2</sub> alkyl), -(C<sub>1</sub>-C<sub>2</sub> alkylene)amino, and -(C(O))(C<sub>1</sub>-C<sub>4</sub> alkyl).

11. (previously presented) A compound according to claim 9 wherein said substituents are selected, independently, from fluoro, chloro, bromo, iodo, C<sub>1</sub>-C<sub>4</sub> alkoxy, trifluoromethyl, C<sub>1</sub>-C<sub>6</sub> alkyl which may optionally be substituted with one hydroxy, C<sub>1</sub>-C<sub>4</sub> alkoxy or fluoro group and which may optionally contain one carbon-carbon double or triple bond, -(C<sub>1</sub>-C<sub>4</sub> alkylene)O(C<sub>1</sub>-C<sub>2</sub> alkyl), C<sub>1</sub>-C<sub>3</sub> hydroxyalkyl, hydroxy, formyl, -COO(C<sub>1</sub>-C<sub>2</sub> alkyl), -(C<sub>1</sub>-C<sub>2</sub> alkylene)amino, and -(C(O))(C<sub>1</sub>-C<sub>4</sub> alkyl).

12. (previously presented) A compound according to claim 1, wherein said compound is

4-(1-ethyl-propoxy)-2,5-dimethyl-6-(2,4,6-trimethyl-benzyl)-pyrimidine;  
[2,5-dimethyl-6-(2,4,6-trimethyl-phenoxy)-pyrimidin-4-yl](1-ethyl-propyl)-amine;  
(1-ethyl-propyl)-[2-methyl-5-nitro-6-(2,4,6-trimethyl-pyridin-3-yloxy)-pyrimidin-4-yl]-amine;  
(N-(1-ethyl-propyl)-2-methyl-5-nitro-N'-(2,4,6-trimethyl-pyridin-3-yl)-pyrimidine-4,6-diamine;  
4-(1-ethylpropoxy)-2,5-dimethyl-6-(2,4,6-trimethylphenoxy)-pyrimidine;  
N-butyl-N-ethyl-2,5-dimethyl-N'-(2,4,6-trimethylphenyl)-pyrimidine-4,6-diamine; or  
6-(1-ethyl-propoxy)-2-methyl-N4-(2,4,6-trimethyl-phenyl)-pyrimidine-4,5-diamine;  
or a pharmaceutically acceptable salt of one of the above compounds.

13-28. (cancelled)

29 (previously presented ). A compound as claimed in claim 1 wherein R<sub>24</sub> and R<sub>25</sub> are selected from -CF<sub>3</sub>, -CHF<sub>2</sub>, CF<sub>2</sub>CF<sub>3</sub>, and CH<sub>2</sub>CF<sub>3</sub>.

30 (cancelled)

31 (currently amended) A pharmaceutical composition ~~as claimed in claim 13~~ for treatment of an inflammatory disorder selected from the group consisting of rheumatoid arthritis and osteoarthritis in a mammal, comprising an amount of a compound according to claim 1 that is effective in the treatment of such disorder, and a pharmaceutically acceptable carrier.

32 (currently amended). A pharmaceutical composition ~~as claimed in claim 14~~ for treatment of depression, selected from the group consisting of major depression, single episode depression, recurrent depression, and child abuse induced depression in a mammal, comprising an amount of a compound according to claim 1 that is effective in the treatment of depression, and a pharmaceutically acceptable carrier.

33 (currently amended) A pharmaceutical composition ~~as claimed in claim 14~~ for treatment of neurodegenerative diseases selected from the group consisting of Alzheimer's disease, Parkinson's disease and Huntington's disease in a mammal, comprising an amount of a compound according to claim 1 that is effective in the treatment of such neurodegenerative diseases, and a pharmaceutically acceptable carrier.

34 (currently amended) A pharmaceutical composition ~~as claimed in claim 14~~ for treatment of chemical dependencies or addictions, selected from the group consisting of dependencies or addictions to alcohol, cocaine, heroin, benzodiazepines, or other drugs in a mammal, comprising an amount of a compound according to 1 that is effective in the treatment of such chemical dependencies or addictions, and a pharmaceutically acceptable carrier.

35 (currently amended) A pharmaceutical composition ~~as claimed in claim 14~~ for treatment of cerebral ischemia in a mammal, comprising an amount of a compound according to claim 1 that is effective in the treatment of cerebral ischemia, and a pharmaceutically acceptable carrier.

36 (currently amended). A pharmaceutical composition ~~as claimed in claim 14~~ for treatment of immune dysfunctions induced by stress selected from the group consisting of porcine stress syndrome, bovine shipping fever, equine paroxysmal fibrillation, confinement dysfunction in chicken, sheering stress in sheep, and human animal interaction stress in dogs, comprising an amount of a compound according to claim 1 that is effective in the treatment of such immune dysfunctions, and a pharmaceutically acceptable carrier.

37 (currently amended) A pharmaceutical composition ~~as claimed in claim 14~~ for treatment of fibromyalgia in a mammal, comprising an amount of a compound according to claim 1 that is effective in the treatment of fibromyalgia, and a pharmaceutically acceptable carrier.

38 (currently amended) A pharmaceutical composition ~~as claimed in claim 14~~ for treatment of anorexia or bulimia nervosa in a mammal, comprising an amount of a compound according to claim 1 that is effective in the treatment of anorexia or bulimia nervosa, and a pharmaceutically acceptable carrier.

39 (currently amended). A pharmaceutical composition ~~as claimed in claim 14~~ for treatment of cerebral ischemia, selected from the group consisting of



cerebral hippocampal ischemia in a mammal, comprising an amount of a compound according to claim 1 that is effective in the treatment of cerebral hippocampal ischemia, and a pharmaceutically acceptable carrier.

40 (currently amended). A pharmaceutical composition ~~as claimed in claim 14~~ for treatment of social phobia, agoraphobia, or specific phobias in a mammal, comprising an amount of a compound according to claim 1 that is effective in the treatment of such phobias, and a pharmaceutically acceptable carrier.

41 (currently amended). ~~The~~ A pharmaceutical composition according to claim 13 wherein the pain perception is for treatment of fibromyalgia in a mammal, comprising an amount of a compound according to claim 1 that is effective in the treatment of fibromyalgia, and a pharmaceutically acceptable carrier.

42 (currently amended). ~~The~~ A pharmaceutical composition according claim 13 wherein the ischemic neuronal damage is for treatment of cerebral ischemia in a mammal, comprising an amount of a compound according to claim 1 that is effective in the treatment of cerebral ischemia, and a pharmaceutically acceptable carrier.

43 (currently amended). ~~The~~ A pharmaceutical composition according to claim 14 for the treatment of depression or postpartum depression in a mammal, comprising an amount of a compound according to claim 1 that is effective in the treatment of such depression, and a pharmaceutically acceptable carrier.

44-45 (cancelled).

46. (previously presented) The compound of claim 1, wherein Z is NH, O, S, NC(OC)CF<sub>3</sub>, or CR<sub>13</sub>R<sub>14</sub>.

47. (previously presented) The compound of claim 46, wherein Z is NH, S, NC(OC)CF<sub>3</sub>, or CR<sub>13</sub>R<sub>14</sub>.

48. (previously presented) The compound of claim 46, wherein Z is NH.

REMARKS

This is in response to the Official Action of April 20, 2005 for the above-captioned application. Claims 1-12, 29 and 31-48 are allowed.


To expedite prosecution, Applicants hereby cancel Claims 13, 14 and 30, without prejudice to the filing of claims directed to the subject matter of Claims 13, 14 and/or 30 in separate applications. Claims 31-43 have been amended to change the claim dependencies and to recite in each case that the composition is a composition comprising an amount of a compound according to claim 1 that is effective in the treatment of the condition recited in each case. Claims 44-45 have been cancelled.

In view of the foregoing, allowance of all pending claims in the application is respectfully requested.

Please charge any appropriate fee to cover this submission to Pfizer Deposit Account No. 16-1445. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

Date: June 23, 2005

  
\_\_\_\_\_  
Andrea E. Dorigo  
Attorney for Applicant(s)  
Reg. No. 47,532

Pfizer, Inc.  
Patent Department, 5th Floor  
150 East 42nd Street  
New York, NY 10017-5755  
(212) 733-1898